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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/350,518	07/09/1999	JOHN C. REED	P-LJ-3578	8259
23601	7590	08/16/2004	EXAMINER	
CAMPBELL & FLORES LLP 4370 LA JOLLA VILLAGE DRIVE 7TH FLOOR SAN DIEGO, CA 92122			HOLLERAN, ANNE L	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 08/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/350,518

Applicant(s)

REED, JOHN C.

Examiner

Anne Holleran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 16 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 11-14, 16, 20-27, 32-34, 36, 37, 44 and 50-66 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11-14, 16, 20-27, 32-34, 36, 37, 44 and 50-66 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. The amendment filed April 16, 2004 is acknowledged. Claims 16, 20, 25, 27, 34, and 44, were amended.

Claims 11-14, 16, 20-27, 32-34, 36, 37, 44, and 50-66 are pending and examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections Withdrawn:***

3. The rejection of claims 11-14, 16, 20-27, 32-34, 36, 37, 44, and 50-66 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment to the claims.

#### ***Rejections Maintained and New Grounds of Rejection:***

4. The rejection of claims 11-14, 16, 20-27, 32-34, 36, 37, 44, and 50-66 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record.

Applicant's arguments have been carefully considered but are unpersuasive. Applicants argue that the full scope of the claims is enabled by the specification and that the references provided in an appendix demonstrate similar statistical methods and that the skill in the art is

quite high. With respect to the enablement of methods in body fluids, applicant has amended the claims to contain the limitation that the methods encompass measuring Bag-1 levels in tumor cells from a body fluid. However, with respect to determining a reference level, applicants' arguments that the combination of the high level of skill in the art with the teachings of the specification allow one to practice the full scope of the claimed inventions. The argument is not found persuasive because the passages cited refer to prophetic reference levels. An actual population of people who might provide samples from which the reference values could be obtained is not described or exemplified. Additionally, when the methods and data provided in the specification are compared to the references provided by applicant, one can see that the situations described in the references are not analogous to the teachings of the specification. In Kim, the reference level was derived from a set of 10 patients that did not have cancer, whereas the one example provided in the specification teaches that the cut-off H-score is a score derived by analyzing only the set of cancer patients for which the methods were being used to prognostic survival. Therefore, the technique used in Kim would not be predictive of what should be used in for practice of the instant application. What population of patients should constitute the control population? In the instant case, cancer patients are not compared to non-cancer patients or any other type of patient. Furthermore, Kim actually teaches that clinical correlation of prognostic factors with the measurement of a protein expression is not settled in the art, primarily because there does not appear, in the case of c-erbB-2, a consensus of what constitutes "over-expression" and what does not (see page 95, 2<sup>nd</sup> column, "c-erbB-2 overexpression ranging as widely as 9-72%"). Secondly, applicant also cited Borre, which categorized Ki-67 expression in cancer patients as "high" or "low", and taught a method where the cut-off was a median score

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(above median was “high”, and below median was “low”). In the instant case, the cut-off H-score of 150 is provided, but it is not taught where this score falls in the continuum of H-scores. Is it a median score or is the cut-off somewhere else? Is the value of the H-score the important factor, or where this score falls in the continuum of population scores?

The rejection of the claimed inventions is maintained because the teachings of the specification are not commensurate in scope with the scope of the claims and because the exemplified method does not provide the skilled artisan with a reasonable expectation of success in practicing the claimed method in view of the teachings in the Kim that choice of a reference level greatly affects the outcome of a prognostic method and in view of the fact that although a cut-off H-score was provided as an example, the specification fails to teach whether this was a median score or a score that fell somewhere else in the continuum of H-scores.

### ***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran  
Patent Examiner  
August 6, 2004

  
**ALANA M. HARRIS, PH.D.**  
**PRIMARY EXAMINER**  
8/9/2004